**AMENDMENTS TO THE SPECIFICATION**

Please amend the title of the application as follows:

THERAPIES FOR ~~RENAL FAILURE~~ GLOMERULONEPHRITIS USING INTERFERON-BETA-1

Please replace the second paragraph bridging pages 8 and 9, with the following amended paragraph:

" Percent identity" or "percent similarity" refer to the sequence similarity between two polypeptides, molecules, or between two nucleic acids. When a position in both of the two compared sequences is occupied by the same base or amino acid monomer subunit, then the respective molecules are identical at that position. The percentage identity between two sequences is a function of the number of matching or identical positions shared by the two sequences divided by the number of positions compared × 100. For instance, if 6 of 10 of the positions in two sequences are matched or are identical, then the two sequences are 60% homologous. By way of example, the DNA sequences CTGACT and CAGGTT share 50% homology (3 of the 6 total positions are matched). Generally, a comparison is made when two sequences are aligned to give maximum identity. Such alignment can be provided using, for instance, the method of Karlin and Altschul described in more detail below. When referring to a nucleic acid, "percent homology" and "percent identity" are used interchangeably, whereas when referring to a polypeptide, "percent homology" refers to the degree of similarity, where amino acids representing conserved substitutions of other amino acids are considered identical to these other amino acids. A "conservative substitution" of a residue in a reference sequence is a replacement with an amino acid that is physically or functionally similar to the corresponding reference residue, e.g., that have a similar size, shape, electric charge, chemical properties, including the ability to form covalent or hydrogen bonds, or the like. Particularly preferred conservative substitutions are those fulfilling the criteria defined for an "accepted point mutation" in Dayhoff et al., 5: Atlas of Protein Sequence and Structure, 5: Suppl. 3, chapter 22: 354-352, Nat. Biomed. Res. Foundation, Washington, D.C. (l978). The percent homology or

identity of two amino acids sequences or two nucleic acid sequences can be determined using the alignment algorithm of Karlin and Altschul (Proc. Nat. Acad. Sci., USA 87: 2264 (1990) as modified in Karlin and Altschul (Proc. Nat. Acad. Sci., USA 90: 5873 (1993). Such an algorithm is incorporated into the NBLAST or XBLAST programs of Altschul et al., J. Mol. Biol. 215: 403 (1990). BLAST searches are performed with the NBLAST program, score = 100, wordlength = 12, to obtain nucleotide sequences homologous to a nucleic acid of the invention. BLAST protein searches are performed with the XBLAST program, score = 50, wordlength = 3, to obtain amino acid sequences homologous to a reference polypeptide. To obtain gapped alignments for comparisons, gapped BLAST is used as described in Altschul et al., Nucleic Acids Res., 25: 3389 (1997). When using BLAST and Gapped BLAST, the default parameters of the respective programs (XBLAST and NBLAST) are used. See the NCBI website at ncbi.nlm.nih.gov. ~~http://www/ncbi.nlm.nih.gov.~~

Please replace the second paragraph on page 25, lines 7-16, with the following amended paragraph:

In one embodiment, a pegylated IFN-β is prepared as follows. IFN-β, e.g., IFN-β-1a bulk intermediate (a clinical batch of bulk drug that passed all tests for use in humans) at 250 μg/ml in 100 mM sodium phosphate pH 7.2, 200 mM NaCl is diluted with an equal volume of 100 mM MES pH 5.0, and the pH was adjusted to 5.0 with HCl. The sample is loaded onto an SP-~~Sepharose~~SEPHAROSE® FF gel filtration column (Pharmacia, Piscataway, NJ) at 6 mg IFN-β/ml resin. The column is washed with 5 mM sodium phosphate pH 5.5, 75 mM NaCl, and the product is eluted with 30 mM sodium phosphate pH 6.0, 600 mM NaCl. Elution fractions can be analyzed for their absorbance values at 280 nm and the concentration of interferon in the samples estimated from the absorbance using an extinction coefficient of 1.51 for a 1 mg/ml solution.

Please replace the paragraph bridging pages 25 and 26 with the following amended paragraph:

To a 1 mg/ml solution of the IFN-β from the SP eluate, 0.5 M sodium phosphate pH 6.0 is added to 50 mM, sodium cyanoborohydride (Aldrich, Milwaukee, WI) is added to 5 mM, and 20K PEG aldehyde (Shearwater Polymers, Huntsville, AL) is added to 5 mg/ml. The sample is incubated at room temperature for 20 hours. The pegylated interferon is purified from reaction products by sequential chromatography steps on a ~~Superose~~SUPEROSE® 6 FPLC sizing column (Pharmacia) with 5 mM sodium phosphate pH 5.5, 150 mM NaCl as the mobile phase and SP-~~Sepharose~~SEPHAROSE® FF gel filtration resin. The sizing column results in base line separation of modified and unmodified IFN-β. The PEG-interferon beta-containing elution pool from gel filtration is diluted 1:1 with water and loaded at 2 mg interferon beta /ml resin onto an SP-~~Sepharose~~SEPHAROSE® gel filtration column. The column is washed with 5 mM sodium phosphate pH 5.5, 75 mM NaCl and then the pegylated interferon beta is eluted from the column with 5 mM sodium phosphate pH 5.5, 800 mM NaCl. Elution fractions are analyzed for protein content by absorbance at 280 nm. The pegylated interferon concentration is reported in interferon equivalents as the PEG moiety did not contribute to absorbance at 280 nm. These method and characterization of the pegylated IFN-β obtained are further described in WO 00/23114. PEG conjugation of IFN-β does not appear to alter its antiviral activity. In addition, the specific activity of pegylated IFN-β was found to be much greater (about 10 times) than that of the non-pegylated IFN-β (WO 00/23114).

Please replace the paragraph on page 26, lines 6-16, with the following amended paragraph:

A 20 kDa mPEG-O-2-methylpropionaldehyde-modified IFN-β can be prepared as follows. 10 mL of IFN-β-1a bulk intermediate (a clinical batch of bulk drug that passed all tests for use in humans) at 250 μg/mL in 100 mM sodium phosphate pH 7.2, 200 mM NaCl is diluted with 12 mL of 165 mM MES pH 5.0 and 50 μL of 5 N HCl. The sample is loaded onto a 300 μL SP-~~Sepharose~~SEPHAROSE® FF gel filtration column (Pharmacia). The column is washed with 3 × 300 μL of 5 mM sodium phosphate pH 5.5, 75 mM NaCl, and the protein is eluted with 5 mM sodium phosphate pH 5.5, 600 mM NaCl. Elution fractions are analyzed for their absorbance at 280 nm and the concentration of IFN-β in the samples estimated using an

extinction coefficient of 1.51 for a 1 mg/mL solution. The peak fractions are pooled to give an IFN-β concentration of 3.66 mg/mL, which is subsequently diluted to 1.2 mg/mL with water.

Please replace the paragraph on page 26, lines 17-33, with the following amended paragraph:

To 0.8 mL of the IFN-β from the diluted SP-~~Sepharose~~SEPHAROSE® gel filtration eluate pool, 0.5 M sodium phosphate pH 6.0 is added to 50 mM, sodium cyanoborohdride (Aldrich) is added to 5 mM, and 20 kDa mPEG-O-2-methylpropionaldehyde is added to 5 mg/mL. The sample is incubated at room temperature for 16 h in the dark. The PEGylated IFN-β is purified from the reaction mixture on a 0.5 mL SP-~~Sepharose~~SEPHAROSE® FF gel filtration column as follows: 0.6 mL of the reaction mixture is diluted with 2.4 mL 20 mM MES pH 5.0, and loaded on to the SP-~~Sepharose~~SEPHAROSE® gel filtration column. The column is washed with sodium phosphate pH 5.5, 75 mM NaCl and then the PEGylated IFN-β is eluted from the column with 25 mM MES pH 6.4, 400 mM NaCl. The PEGylated IFN-β is further purified on a Superose 6 HR 10/30 FPLC sizing column with 5 mM sodium phosphate pH 5.5, 150 mM NaCl as the mobile phase. The sizing column (25 mL) is run at 20 mL/h and 0.5 mL fractions are collected. The elution fractions are analyzed for protein content by absorbance at 280 nm, pooled, and the protein concentration of the pool determined. The PEGylated IFN-β concentration is reported in IFN equivalents as the PEG moiety does not contribute to absorbance at 280 nm. Samples of the pool are removed for analysis, and the remainder can be diluted to 30 μg/mL with HSA-containing formulation buffer, aliquoted at 0.25 mL/vial, and stored at –70 °C.

Please replace the paragraph on page 27, lines 1-29, with the following amended paragraph:

20 kDa mPEG-O-*p*-phenylacetaldehyde-modified IFN-β can be prepared as follows. 20 mL of ®IFN-ß bulk intermediate (a clinical batch of bulk drug that passed all tests for use in humans) at 250 μg/mL in 100 mM sodium phosphate pH 7.2, 200 mM NaCl is diluted with 24 mL of 165 mM MES pH 5.0, 100 μL of 5 N HCl, and 24 mL water. The sample is loaded onto a

600 µL SP-~~Sepharose~~SEPHAROSE® FF gel filtration column (Pharmacia). The column is washed with 2 × 900 µL of 5 mM sodium phosphate pH 5.5, 75 mM NaCl, and the protein is eluted with 5 mM sodium phosphate pH 5.5, 600 mM NaCl. Elution fractions are analyzed for their absorbance at 280 nm and the concentration of IFN-β in the samples was estimated using an extinction coefficient of 1.51 for a 1 mg/mL solution. The peak fractions are pooled to give an IFN-ß concentration of 2.3 mg/mL. To 1.2 mL of the IFN-β-1a from the SP-~~Sepharose~~SEPHAROSE® gel filtration eluate pool, 0.5 M sodium phosphate pH 6.0 is added to 50 mM, sodium cyanoborohdride (Aldrich) is added to 5 mM, and 20 kDa mPEG-O-*p*-phenylacetaldehyde, is added to 10 mg/mL. The sample is incubated at room temperature for 18 h in the dark. The PEGylated IFN-β can be purified from the reaction mixture on a 0.75 mL SP-~~Sepharose~~SEPHAROSE® FF gel filtration column as follows: 1.5 mL of reaction mixture is diluted with 7.5 mL 20 mM MES pH 5.0, 7.5 mL water, and 5 µL 5 N HCl, and loaded onto the SP-~~Sepharose~~SEPHAROSE® gel filtration column. The column is washed with sodium phosphate pH 5.5, 75 mM NaCl and then the PEGylated IFN-β is eluted from the column with 20 mM MES pH 6.0, 600 mM NaCl. The PEGylated IFN-β is further purified on a Superose 6 HR 10/30 FPLC sizing column with 5 mM sodium phosphate pH 5.5, 150 mM NaCl as the mobile phase. The sizing column (25 mL) is run at 20 mL/h and 0.5 mL fractions are collected. The elution fractions are analyzed for protein content by absorbance at 280 nm, pooled, and the protein concentration of the pool determined. The PEGylated IFN-β concentration is reported in IFN equivalents after adjusting for the contribution of the PEG (20 kDa mPEG-O-*p*-phenylacetaldehyde has an extinction coefficient at 280 nm of 0.5 for a 1 mg/mL solution) to the absorbance at 280 nm using an extinction coefficient of 2 for a 1 mg/mL solution of the PEGylated IFN-β. Samples of the pool can be removed for analysis, and the remainder can be diluted to 30 µg/mL with HSA-containing formulation buffer, aliquoted at 0.25 mL/vial, and stored at −70 °C.

Please replace the paragraph on page 57, lines 13-23, with the following amended paragraph:

IFN-β used in this study was rat IFN-β corresponding to amino acids 22-184 of GenBank Accession No. P70499. Rat IFN-β was expressed in Chinese Hamster Ovary (CHO) S-32 cells adapated to growth in suspension and secreted into the culture medium. The cells were grown in serum-containing medium in fermentor cultures. IFN-β was purified from conditioned culture medium using sequential chromatography on Pharmacia SP-~~Sepharose~~SEPHAROSE® gel filtration resin, Blue ~~Sepharose~~SEPHAROSE® gel filtration resin, and Superose 12 resins, and Biorad Bio-Scale Ceramic Hydroxyapatite and Bio-Scale S resins. The IFN-β was then dialyzed extensively against 25 mM citrate/150 mM NaCl (pH 4.5) and filter-sterilized (0.2 μm). The IFN-β preparation was >99% pure as determined by densitometry of Coomassie-stained non-reducing SDS-PAGE gels. The specific activity was determined to be about $3 \times 10^8$ units/mg as measured on rat RATEC cells.

Please replace the paragraph on page 58, lines 20-31, with the following amended paragraph:

Glomerular fibrosis: the % renal cortical areas stained green by Masson-Trichrome histochemistry which offers a way of assessing collagen "load" within a kidney, was estimated by computer. Individual glomeruli can also be selected as the area of interest to calculate specific glomerular fibrosis. To quantify interstitial fibrosis within glomeruli, paraffin-embedded kidney sections were stained using a standard trichrome method (Martius Yellow, Brilliant Crystal Scarlet and Aniline Blue). To quantify glomerular fibrin deposition (e.g., fibrinoid necrosis) , paraffin-embedded kidney sections were stained using Martius Yellow which stains fibrin a red/orange color. Sections were examined under X200 magnification using an Olympus BX40 microscope (Olympus Optical, London, U.K.) mounted with a Photonic digital camera (Photonic Science, East Sussex, U.K.). Images were captured and analyzed using ~~Image-Pro Plus~~IMAGE-PRO PLUS™ software (Media Cybernetics, Silver Spring, MD).